

U.S. DEPARTMENT OF COMMERCE
National Technical Information Service

PB-259 699-T

**Comparative Effectiveness of Some
Aminoalkylphosphonic Acids in
Excretion of Berillium from Rats**

Environmental Protection Agency, Research Triangle Park, N C

1972

BIBLIOGRAPHIC DATA SHEET	1. Report No. EPA TR73-144	2.	3. Recipient's Accession No.
4. Title and Subtitle Comparative effectiveness of some aminoalkylphosphonic acids in excretion of Berillium from rats.		5. Report Date 1972	
7. Author(s) A.T. Ivannikov, P.F. Burgryshev, A.A. Kuznetsov		8. Performing Organization Rept. No.	
9. Performing Organization Name and Address TRANSLATED FROM RUSSIAN BY EPA		10. Project/Task/Work Unit No.	
		11. Contract/Grant No.	
12. Sponsoring Organization Name and Address Translation Service Office of Administration - Library Research Triangle Park, NC 27711		13. Type of Report & Period Covered	
		14.	
15. Supplementary Notes GIG. TR. PROF. ZABOL. 16(4): 55-57, 1972			
16. Abstracts			
17. Key Words and Document Analysis. 17a. Descriptors EPAISD			
17b. Identifiers/Open-Ended Terms OCCUPATIONAL HEALTH			
17c. COSATI Field/Group 06J 57U /			
18. Availability Statement THIS TRANSLATION WAS MADE FROM A NON-COPYRIGHTED TEXT.		19. Security Class (This Report) UNCLASSIFIED	21. No. of Pages 8
		20. Security Class (This Page) UNCLASSIFIED	22. Price 3.50/3.00

APTC 48039

COMPARATIVE EFFECTIVENESS OF SOME AMINOALKYLPHOSPHONIC
ACIDS IN EXCRETION OF BERILLIUM FROM RATS
[Sravnitel'naya effektivnost' nekotorykh aminoalkilfosfonovykh
kislot v vyvedenii berilliya iz organizma krysa]

by

A. T. Ivannikov, P. F. Bugryshev, A. A. Kuznetsov
(Moscow) of the Institute of Biophysics

Published in Gig. Tr. Prof. Zabol.
[Industrial Hygiene and Occupational Diseases]
Vol. 16, No. 4, 1972, pp. 55-57.

The authors study the effect of two aminoalkylphosphonic acids on the excretion of berillium from rats. It is discovered that the acids' effect on berillium excretion varies according to the number of times they are administered, the period after berillium intake at which they are administered and also according to the specific organ or tissue in which accumulation of berillium is measured.

When they enter the organism of workers, berillium and its compounds may cause specific diseases of varying degrees of severity. In connection with this, the question of seeking remedies that will accelerate excretion of berillium from the main organs in which it is deposited is of no small

Translated for Air Pollution Technical Information Center from the Russian by
LEO KANNER ASSOCIATES, P. O. Box 5187, Redwood City, California 94063
(415) 365-3046, October 1972.

importance. A number of works have been published in recent years devoted to the use of aminoalkylphosphonic acids during incorporation of berillium. These works have shown the definite effectiveness of this class of compounds in accelerating excretion of berillium from animal organisms (O. G. Arkhipov et al., 1964, 1966, 1967).

We have studied the influence of two aminoalkylphosphonic compounds, phosphycin and $\text{Na}_3\text{Ca}_2\text{-DTPP}$ [TPP-thiamine pyrophosphate], on excretion of incorporated berillium depending on the period at which the preparations are administered and the number of times they are administered.

Methods.

Experiments were conducted on 45 albino rats 170-180 g in weight. All the animals were divided into 9 groups, 5 rats in each. We administered $3 \cdot 10^{-6}$ mg of Be^7 in the form of a chloride, together with the stable berillium chloride that was present, intraperitoneally to the rats, 0.5 ml each, in a quantity of 4 millicuries per rat. We administered DTPP and phosphycin (each separately) intraperitoneally, figuring 500 mg per 1 kg of rat weight, at the following periods: 2 minutes, 1 hour and 4 hours after injection of Be^7Cl_2 . We studied the influence of multiple use of the preparations on rats of two groups. For this, we administered phosphycin and DTPP three times, 4 hours, 1 day and 2 days after injection of berillium. Three days after administration of Be^7Cl_2 we slaughtered the rats and determined the content of radioactivity in specimens taken from organs and tissues. We determined the radioactivity of the specimens according to gamma-radiation by the comparative method using a scintillation counter with a NaI crystall.

We expressed the Be^7 content in the organs of control and experimental

animals in percentages of the administered quantity and also expressed it in the experimental animals in percentages of the control. We expressed the radioactivity of rats' bodies, as measured by gamma-radiation, in percentages of the radioactivity of each animal as measured immediately after administration of Be^{7}Cl_2 . The magnitudes of isotope content in organs and tissues presented in Tables 1 and 2 represent arithmetic means from data obtained in examination of 5 rats at each period.

Table 1. The influence of DTPP and phosphycin on intensity of gamma-radiation in the bodies of rats subjected to Be^{7}Cl_2 charging.

a Препарат	b Срок введения после заправки	1-й сутки		2-й сутки		3-й сутки	
		% от введенной активности	% от контроля	% от введенной активности	% от контроля	% от введенной активности	% от контроля
h Контроль		83,3 ± 3,7	100	76,5 ± 4,5	100	72,7 ± 4,3	100
i DTPP	Через 2 мин.	18,5 ± 3,0	22,2	11,8 ± 2,4	15,4	10,1 ± 1,8	13,9
j фосфин	То же	35,0 ± 3,0	42,0	31,2 ± 2,2	40,8	29,2 ± 2,0	40,2
i DTPP	Через 1 час	51,5 ± 3,0	61,8	46,2 ± 2,3	60,4	44,3 ± 1,6	60,9
j фосфин	То же	54,4 ± 2,0	65,3	49,0 ± 1,4	64,1	46,7 ± 1,9	64,2
i DTPP	Через 4 часа	74,3 ± 4,3	89,2	65,0 ± 3,4	85,0	61,5 ± 3,0	84,6
j фосфин	То же	70,5 ± 2,3	84,6	63,4 ± 2,1	83,9	60,6 ± 2,1	83,4
i DTPP	Троекратно через 4 часа, 1 и 2 суток	74,2 ± 1,2	89,1	67,6 ± 0,22	88,4	62,0 ± 1,1	85,3
j фосфин	То же	73,5 ± 2,0	88,2	63,8 ± 1,9	83,4	59,8 ± 2,8	82,3

Key: a. preparation; b. period at which administered after charging; c. % of administered radioactivity; d. % of control; e. first day; f. second day; g. third day; h. control; i. DTPP; j. phosphycin; k. after 2 minutes; l. same; m. after 1 hour; n. after 4 hours; o. 3 times after 4 hours, 1 day and 2 days.

Table 1 presents results of the experiment according to the Be^{7} content in the bodies of rats according to gamma-activity. The main quantity of beryllium (16.7% of the administered quantity) is excreted from the organisms of control animals during the first day. The maximum effect is observed when

Table 2. Be⁷ content in organs of rats with administration of DTPP and phosphycin.

Подготовка	Срок введения после загрузки	Селект		Печень		Селект		Печень		Печень	
		% от введенного	% от контроля	% от введенного	% от контроля	% от введенного	% от контроля	% от введенного	% от контроля	% от введенного	% от контроля
Контроль ①		34,2 ± 7,8	100	16,8 ± 3,9	100	1,1 ± 0,28	100	2,1 ± 0,42	100		
ДТПФ ②	2 мин	8,2 ± 0,82	24,0	0,59 ± 0,047	3,5	0,045 ± 0,01	4,1	1,3 ± 0,53	61,9		
	1 час	33,3 ± 2,0	97,4	5,4 ± 0,45	32,1	0,23 ± 0,04	20,9	2,9 ± 0,23	138,1		
	4 часа	31,3 ± 2,1	100	8,9 ± 1,1	53,0	0,48 ± 0,11	43,6	2,8 ± 0,32	133,3		
	4 часа, 1 и 2 суток	27,3 ± 2,6	79,8	7,1 ± 0,56	42,3	0,4 ± 0,09	36,4	2,9 ± 0,15	136,1		
Фосфин ③	2 мин	35,7 ± 3,6	104,4	0,72 ± 0,12	4,3	0,03 ± 0,003	2,7	0,34 ± 0,03	16,2		
	1 час	41,9 ± 2,5	122,5	6,3 ± 0,73	37,5	0,19 ± 0,01	17,3	2,3 ± 0,4	109,5		
	4 часа	37,1 ± 4,2	108,5	12,2 ± 3,6	72,6	0,4 ± 0,11	36,4	2,2 ± 0,32	101,8		
	4 часа, 1 и 2 суток	38,6 ± 1,6	113,5	10,0 ± 1,2	59,5	0,45 ± 0,061	40,9	2,2 ± 0,16	104,8		

4

Key: a. preparation; b. period after charging at which administered; c. % of administered; d. % of control; e. skeleton; f. liver; g. spleen; h. kidney; i. control; j. DTPP; k. phosphycin; l. 2 minutes; m. 1 hour; n. 4 hours; o. 4 hours, 1 day and 2 days.

phosphycin and DTPP are administered two minutes after injection of Be^7Cl_2 . When the preparations were administered 1 and 4 hours after injection their effectiveness decreased markedly. From the point of view of their influence on berillium excretion, the difference between phosphycin and DTPP leveled out at the specified periods after administration.

The data, presented in Table 2, on the berillium content in the main organs in which it is deposited confirmed the fundamental regularities revealed during change in the gamma-activity of the animals' bodies. DTPP decreased the Be^7 content to 1.3 and 8.2% of the administered quantity (62 and 24% of the control) in the kidneys and skeleton respectively. Phosphycin exerted a more substantial influence than DTPP on decrease in the content of the isotope in the kidneys (to 0.34% of the administered quantity or 16.2% of the control), but did not influence its content in the skeleton.

The preparations' effect on prevention of the isotope's lodging in the liver and spleen was less pronounced when they were administered once 1 and 4 hours after injection of Be^7Cl_2 ; they exerted no influence at all on decrease in berillium content in the kidneys and skeleton. In 3-fold administration, the preparations proved somewhat more effective in berillium excretion than in single use. This was more clearly pronounced with administration of DTPP. The decrease in the preparations' effectiveness with increase in the period after administration of Be^7Cl_2 gives us a basis for saying that early use of aminoalkylphosphonic acids is necessary when berillium gets into the organism.

DTPP proved more effective than phosphycin in repeated administration at later periods.

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